

Early Onset of Antidepressant Action: Impact on Primary Care

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Although the prevalence of depression among patients in primary care is high, the primary care system is inefficient at recognizing and managing this disorder. The delayed onset of antidepressant effect contributes to this problem, since patients and physicians may prematurely discontinue a medication that is not perceived as effective. The undertreatment of depression has profound effects on patients, the health care system, and society. The development of antidepressants with a faster onset of action would improve the pharmacologic management of depression and have wide-ranging benefits for the health care system.
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Antidepressants typically require from 2 to 12 weeks to exert their therapeutic effects. This delayed onset of action contributes significantly to the undertreatment of depression in primary care settings. The development of treatment strategies or new antidepressants with early onset of action might improve treatment of depression and have beneficial effects on the relationships between physician and patient, patient and family, and physician and health care system. This review will discuss the treatment of depression in the primary care system and outline the benefits of an antidepressant with an early onset of action.

INEFFICIENCY OF DEPRESSION TREATMENT IN PRIMARY CARE: CAUSES AND CONSEQUENCES

The prevalence of major depression in the community at large is 2% to 4%, while in primary care practices it is estimated to be 5% to 12%.¹ In other medical settings in which primary care physicians practice, the prevalence of depression or depressive syndromes is even higher: 10% to 14% among medical inpatients and 6% to 25% among nursing home residents.¹

The primary care system is inefficient at recognizing and managing depression. According to several studies, a little more than half of the primary care patients who meet the criteria for depression receive a proper diagnosis,² while only one third (or less) are treated with an antide-

pressant.^{2,3} Furthermore, despite the well-established efficacy rate of adequate antidepressant pharmacotherapy (60%–70%), few primary care patients receive the recommended doses of medication.³ Finally, most patients in primary care prematurely discontinue treatment with antidepressant drugs, after an average of 2 months of therapy.⁴ Thus, rates of treatment failure, relapse, and recurrence are high even among patients who receive an appropriate diagnosis.

Several factors contribute to the inefficient treatment of depression in primary care. Many patients are concerned with the stigma associated with depression and, as a result, are hesitant to discuss affective symptoms with their physicians. Physicians, on the other hand, are frequently unresponsive to their patients' emotional concerns, in part owing to the time required for diagnosis, patient education, and treatment. Often, poor insurance coverage for the treatment of psychiatric disorders in primary care (such as with mental health "carve-outs" [the subcontracting of mental health care to specialty vendors]) delays antidepressant therapy.

The latency of antidepressant effect compounds these other problems, since it often causes both patients and physicians to decide prematurely that a medication is not effective. From the patient's point of view, the side effects that appear during the first few weeks of pharmacotherapy may not seem to be offset by a significant elevation of mood or by relief of other symptoms. From the physician's perspective, a lack of improvement after a month or more of therapy may suggest that another drug would be more appropriate or that the diagnosis is incorrect. The second scenario, an incorrect diagnosis, is common in the primary care setting, where many physicians substitute clinical impressions for a DSM-IV–based evaluation and thus diagnose depression only after a successful trial of antidepressant medication. After an apparently failed trial, patients

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often are viewed as having a “depressive character” and are not considered for further treatment.

The undertreatment of depression in primary care has profound effects on patients, the health care system, and society. Among patients, unmanaged or inadequately managed depression adversely affects every aspect of life, from relationships with family and friends to job performance to physical health. Depression is associated with increased absenteeism and decreased productivity in the workplace,⁵ increased unnecessary visits to the doctor’s office, and an increased risk of suicide. Among elderly patients, depression appears to be related to accelerated physical decline.⁶ Among patients with chronic medical conditions—who are as much as 3 times more likely than healthy persons to suffer from comorbid depression⁷—improperly managed symptoms of depression are associated with increased morbidity and mortality.^{8,9} It is not surprising that annual health care costs are twice as high for depressed individuals as for the general population.¹⁰

The complex interactions between major depression and diabetes provide a useful model for understanding the global impact of depression treatment on patient outcomes. Major depression is associated with a 1.8% to 3.3% increase in blood hemoglobin A_{1c} levels and elevated overall blood glucose levels among patients with diabetes.¹¹ As a result, diabetic patients with comorbid depression experience 30% to 40% more neuropathy, retinopathy, and nephropathy than nondepressed patients.¹¹ Depression also adversely affects behavior among diabetics, leading to decreased activity, poor adherence to both dietary and pharmacologic treatment recommendations, and delayed care for glucose control and complications. In turn, diabetes may worsen the symptoms of major depression.

Total expenditures for diabetes care in the United States were \$47.9 billion in 1995, including \$18.8 billion for diabetes itself and \$18.7 billion for chronic complications.¹² Although formal quantitative analyses have not been conducted, it is likely that health care costs are very high among diabetic patients with depression, since depression substantially increases the rate of diabetic complications.

POTENTIAL BENEFITS OF EARLY ONSET OF ANTIDEPRESSANT ACTION

A treatment for depression with significantly earlier onset of therapeutic effect would likely improve outcomes among primary care patients through several mechanisms. First, it would improve medication management. If a patient’s early response predicts his or her long-term response, changes in treatment approach due to lack of efficacy would occur in a more timely manner. An antidepressant with an earlier onset of effect would also decrease the unnecessary dosage increases that overshoot the therapeutic level required for some patients. Since such increased dosage, particularly with agents that do not exhibit

linear pharmacokinetics, results in increased rates of side effects and decreased short- and long-term treatment continuation, eliminating upward titration would likely improve outcome.

Early onset of antidepressant efficacy would also prevent premature discontinuation of treatment due to perceived lack of efficacy. Patients’ satisfaction and confidence in their physician and treatment plan would improve. In turn, adherence to treatment recommendations for major depression and any concomitant chronic medical illness would increase.

Faster relief from psychological suffering and major depressive symptoms such as sleep disturbance, fatigue, and poor concentration would directly benefit patients in several ways. First, it would improve general functioning sooner. In cases in which treatment is initiated for recent-onset depression, early antidepressant effect would interrupt the cascade of decreased self-esteem and function that often leads to changes in social role performance and disruption of family, work, and social roles. Second, early onset of antidepressant action would decrease the incidence of self-medication of depressive symptoms and secondary substance abuse.

Improved functioning and adherence to therapy would be especially beneficial for patients with comorbid medical conditions. Several studies^{13,14} have shown that effective antidepressant therapy improves the course of both depression and comorbid illnesses such as diabetes.

For primary care physicians, the availability of an antidepressant treatment regimen with early onset would likely improve their sense of self-efficacy in the care of depression. It might also result in a decreased workload by reducing the number of early-episode office visits made by depressed patients. With the promise of a faster therapeutic effect and a greater assurance that the treatment would be effective in the long term, it is likely that primary care physicians would be more active in identifying major depression and initiating treatment. As a result, more depressed patients would receive adequate treatment.

Finally, early onset of antidepressant effect would benefit employers and society. Work function would return sooner; absenteeism, accidents, and employee turnover would be reduced. It is likely that health care costs would be decreased owing to (1) shortened episodes of depression, (2) decreased rates of somatization and unproductive medical workups, and (3) improvement in chronic medical illness and decreased psychiatric and medical hospitalization.

SUMMARY

Early onset of antidepressant action would improve both the recognition and treatment of major depression in primary care. For the average patient treated with a faster-acting antidepressant, treatment dropouts and progression to chronic major depression would probably decrease.

Faster onset of action also would substantially improve outcomes and quality of care among patients with chronic comorbid medical illness. In addition to improving the health and functioning of patients at home and in the workplace, faster onset of action would lower medical and disability costs and thereby substantially benefit society. From a primary care perspective, developing therapeutic options that decrease the time to onset of antidepressant effect should be a high priority.



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